UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,234	10/24/2003	Claus Lindvald Johansen	674509-2025.1	1385

20999 7590 09/07/2007
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,234	JOHANSEN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12 and 15-32* is/are pending in the application.

4a) Of the above claim(s) *18-21 and 26-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-12,15-17 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 31, 2007 has been entered.

The AF amendment filed July 2, 2007 amending claims 1, 23, 26 and 28 has been entered.

Claims 1, 2, 4-12 and 15-32 are pending. Claims 18-21 and 26-32 have been previously withdrawn.

Claim Objections

Claims 1, 2 and 4-6 are objected to because "quaternary" is misspelled. Claim 2 is further objected to because "Dimethyl" is misspelled on lines 8-9.

Claims 15-17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 15-17 depend from claim 1. Claim recites "a bacterial, yeast or fungal cell comprising ... recombinant POI". Therefore, said cell is a transformed cell (claim 15), said cell

transformed with a nucleic acid encoding POI (claim 16), wherein said recombinant POI is produced by recombinant DNA techniques (claim 17) because by definition, "recombinant" is what produced by "recombinant techniques".

Claim 22 is objected to because "oxidase" is misspelled on line 2.

Claim 25 is objected to because American spelling, i.e. "hybridizing" and "hybridizable" should be used.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-12, 15-17 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, with dependent claims 4-12, 15-17, 22-25, is drawn to a method for releasing any intracellular recombinant protein of interest (POI) using a membrane extracting composition comprising a quaternary ammonium compound. Claims 4-12 recite specific extracting compositions, specific temperatures and pH optimum.

Therefore, the claims are drawn to a method of making of a POI using any quaternary ammonium compound. The genus of quarternary ammonium compounds encompasses unlimited number of species having wildly different structures and properties depending on the structure of the constituents in the quaternary ammonium compound. The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. Structural features that could distinguish compounds in the genus from other quaternary ammonium compounds are missing from the disclosure. The specification does not provide a correlation between the structure and the requisite properties (i.e., the ability to release a POI from a cell) that is common to all members of the quaternary ammonium compounds genus. The specification discloses the use of 7 specific quaternary ammonium compounds containing methylene groups as an extracting agent (page 69, Table 8).

Claim 22 depends from claim 1 and is limited to POI that is HOX (hexose oxidase). The genus of HOXs encompasses any HOX from any source. The specification teaches a single representative species of HOXs, *Chondrus crispus* HOX having the amino acid sequence of SEQ ID NO:23 and encoded by SEQ ID NO:22. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being HOX. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

With regard to a process, a few structurally similar representatives of quaternary ammonium compounds are insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed tremendously diverse genus.

Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1, 4-12, 15-17 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for releasing a recombinant POI using a quaternary ammonium compound selected from the group of compounds recited in claim 2, does not reasonably provide enablement for a method for releasing of a POI using any quaternary ammonium compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for releasing recombinant POI using any quaternary ammonium compound at concentrations 0.05%-6.0%. The art teaches permeabilization of cells and thus, releasing intracellular proteins using a quaternary ammonium compounds such as CTAC, CTAB, LTAB, *etc.*, see below. There is no guidance in the specification as to what are other essential conditions such as temperature and pH, for example, and how the combined experimental conditions change depending on the structure of the POI. The art teaches permeabilization of cells and thus releasing recombinant proteins using a quaternary ammonium compounds such as CTAC, CTAB, LTAB, etc. In every such case finding the right combination of experimental conditions requires trial and error experimentation.

The specification discloses the production of *Chondrus crispus* HOX in the yeasts *Hansenula polymorpha* and *Pichia pastoris* using an engineered DNA of SEQ ID NO:22 that accommodates yeasts codon preferences. The extraction of thus expressed HOX was carried out using the specific quaternary ammonium compounds such as CTAB and LTAB as an extracting agent. The specification teaches the production of two other recombinant proteins from the yeast cells using the same extracting agents.

Without sufficient guidance, beyond that provided, releasing a recombinant POI using any quaternary ammonium compound of an unknown structure is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is confusing as reciting "a nucleotide sequence set out in SEQ ID No 22" because "a" implies several sequences where it appears only one, i.e. the nucleotide sequence of SEQID NO:22 is intended.

Claim 25 recites a sequence complementary sequence that encodes HOX. By definition, a DNA molecule which hybridizes to a coding strand is the complement and therefore, does not, itself, code for the protein in question and its expression would never result in a protein. Furthermore, without knowing the degree of complementarity, the metes and bounds of the claim are unascertainable.

Claim Rejections - 35 USC § 102/§ 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4-12 and 15-17 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sekhar et al.

Sekhar et al (Process Biochemistry (1999) Vol. 34, pages 349-354, form PTO-1449 filed 1/26/04, reference BK) teach preparation of catalase and other enzymes from Bakers' yeast cells permeabilized with CTAB. They teach that in *S. cerevisiae*, catalase is an intracellular enzyme (page 350). They teach that whole cells show very low catalase and other enzyme activity due to the impermeability of the whole cells (page 350).

They teach concentration, time, temperature and pH dependence of catalase activity in CTAB permeabilized yeast cells. The concentration of CTAB comprises the range from about 0.1% to about 0.5% by weight of CTAB as required by claims 4-6 (page 351, Figure 1). The temperature comprises the range from about 4^{O} C to 40^{O} C as required by claims 7-9 and the pH range comprises pH of from about 2.0 to about 11.0 as required by claims 10-12 (page 352, Figure 2). The measure the activity of alcohol dehydrogenase (ADH) and refer and discuss the data for other enzymes disclosed in reference (Gowda et al. (1991) Enzyme Microb. Technol., Vol. 13, pages 154-157, form PTO-1449 filed 1/26/04, reference AL).

The claimed method is based on the permeability of the cells not on the POI being recombinant or native. Furthermore, what is important is that protein is inside the

cell. Further, the protein is the same whether it occurs naturally or is produced recombinantly. Therefore, claims 1, 2, 4-12 and 15-17 are anticipated by the teachings of Sekhar et al. In alternative, it would be obvious to apply the method taught by Sekhar to release any POI from the yeast cells whether said POI is naturally occurring or recombinantly produced in the yeast cells.

Claims 1, 2, 4-12,15-17, 22, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sekhar et al in view of Hansen et al.

The teachings of Sekhar et al are outlined above.

Hansen et al (JBC (1997) Vol. 272 (17), pages 11581-11587, form PTO-1449 filed 1/26/04, reference AN) teach hexose oxidase(HOX) from *Chondrus crispus* and a DNA encoding thereof (page 11581, Figure 3). Its amino acid sequence is 100% identical to SEQ ID NO:23 of the instant invention. The DNA encoding thereof from *Chondrus crispus* (1881 bp) is 77.9% identical to SEQ ID NO:22 of the instant invention that is yeast codon optimized. They teach the production of HOX using *Pichia pastoris* transformed with a DNA encoding HOX (page 11584, 2nd column). Hansen et al teach the importance and industrial applicability of the enzyme.

It would have been obvious to one of ordinary skill in the rat at time the invention was made to apply the method taught by Sekhar et al to release HOX expressed in the yeast, *P.pastoris*. one of ordinary skill in the art would a reasonable expectation of success that said method is applicable to the cells of another yeast, *P. pastoris*. It would

have been also obvious to express HOX in *S. serevisiae* and release it according to the method taught by Sekhar et al.

Response to Arguments

Applicant's arguments filed July 2, 2007have been fully considered but they are not persuasive.

With regard to the objection to the claims, Applicants argue that case that is not necessarily the case that a bacterial, yeast or fungal cell comprising a recombining POI is the same as a transformed cell. For example, a bacterial, yeast or fungal cell comprising a recombining POI could be a descendant of a transformed cell. That is, a bacterial, yeast or fungal cell comprising a recombining POI could be the progeny of a bacterial, yeast or fungal cell that was transformed with a nucleic acid encoding a POI using recombinant DNA techniques as required by claims 15-17" (Remarks, page 7). This is not persuasive because the progeny of a transformed cell is a transformed cell.

With regard to the 112, 1st paragraph rejections, these rejections are reworded in view of the amendment. These rejections are reworded and concentrated on a quaternary ammonium compound that can be used in the invention. It is noted that statement that "The Examples teach that the invention may be performed across a number of different organisms, including *Chondrus crispus*, *Hansenula polymorpha* and *Pichia pastoris*" includes red alga *Chondrus crispus* that naturally produces HOX (Remarks, page 10).

The 112, 1st paragraph new matter rejection is withdrawn in view of the amendment.

The outstanding 112, 2nd paragraph, rejection is withdrawn in view of the amendment.

The outstanding 103(a) rejection is withdrawn in view of the amendment and Applicants remarks indicating that that the claimed method is applied to soluble intracellular proteins not inclusion bodies (pages 13-14).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

August 31, 2007